

Irritation and Local Tissue Tolerance in Pharmaceutical Safety Assessment

Both irritation and local tolerance studies assess the short-term hazard of pharmaceutical agents in the immediate region of their application or installation. In particular, these studies are done (expected) to assess topically or parenterally administered drug formulations (Gad and Chengelis, 1998). Note that these are hazard tests properly performed using the clinical formulation.

Topical local tolerance effects are almost entirely limited to irritation. Though this usually means dermal irritation, it can also be intracutaneous, mucosal, penile, perivascular, vaginal, bladder, rectal, nasal, or ocular, depending on the route of drug administration. All but ocular irritation use some version of a common subjective rating scale (see Table 1) to evaluate responses. The outcome of all of these tests primarily evaluates the response of the first region of tissue (which is exposed to the highest concentration) to an administered drug substance. In general, any factor which enhances absorption through the contacted tissue is likely to decrease tissue tolerance. Zhai et al. (2008) should be referred to for a more detailed coverage of the subject of topical tissue toxicology.

For the skin, this scale is used in the primary dermal irritation test, which is performed for those agents that are to be administered to patients by application